> 10/518914 DT01 Rec'd PCT/PTC 23 DEC 2004

## IN THE CLAIMS:

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Please amend the claims as follows:

- 1. (Original) A method for producing a sustained-release composition, which comprises mixing an aqueous solution containing a physiologically active substance and an acid or base in a molar amount of about 1.5 or more times that of the physiologically active substance with a solution of a biodegradable polymer, and then drying the mixture.
- 2. (Original) The method according to claim 1, wherein the aqueous solution is obtained using a salt of the physiologically active substance with the acid or base.
- 3. (Original) The method according to claim 1, wherein the proportion of the physiologically active substance in the sustained-release composition is about 0.001 to about 50% by weight.
- 4. (Original) A method for stabilizing a mixture of an aqueous solution containing a physiologically active substance and a solution of a biodegradable polymer, which comprises adding an acid or base in a molar amount of about 1.5 mol or more times that of the physiologically active substance.
- 5. (Original) A method for allowing a mixture of an aqueous solution containing a physiologically active substance and a solution of a biodegradable polymer to have a viscosity of about 3,000 cp or less, which comprises adding an acid or base in a molar amount of about 1.5 mol or more times that of the physiologically active substance.
- 6. (Original) The method according to any one of claims 1, 4 and 5, wherein the physiologically active substance is a physiologically active peptide.
- 7. (Original) The method according to claim 6, wherein the physiologically active peptide is an LH-RH derivative.
- 8. (Original) The method according to claim 7, wherein the LH-RH derivative is a compound represented by the general formula:

wherein Y represents DLeu, DAla, DTrp, DSer(tBu), D2Nal or DHis(ImBzl) and Z represents NH-C<sub>2</sub>H<sub>5</sub> or Gly-NH<sub>2</sub>.

- 9. (Original) The method according to any one of claims 1, 4 and 5, wherein the acid or base in a molar amount of about 1.5 to about 5 times that of the physiologically active substance is used.
- 10. (Original) The method according to any one of claims 1, 4 and 5, wherein the acid or base in a molar amount of about 1.65 to about 3 times that of the physiologically active substance is used.
- 11. (Original) The method according to any one of claims 1, 4 and 5, wherein the acid is an organic acid.
- 12. (Original) The method according to claim 11, wherein the organic acid is a fatty acid.
- 13. (Original) The method according to claim 12, wherein the fatty acid is acetic acid.
- 14. (Original) The method according to any one of claims 1, 4 and 5, wherein the biodegradable polymer is an  $\alpha$ -hydroxycarboxylic acid polymer.
- 15. (Original) The method according to claim 14, wherein the  $\alpha$ -hydroxycarboxylic acid polymer is a lactic acid-glycolic acid polymer.
- 16. (Original) The method according to claim 15, wherein the molar ratio of lactic acid to glycolic acid in the lactic acid-glycolic acid polymer is 100:0 to 50:50.
- 17. (Original) The method according to claim 16, wherein the molar ratio of lactic acid to glycolic acid in the lactic acid-glycolic acid polymer is 100:0.
- 18. (Original) The method according to claim 15, wherein the weight average molecular weight of the lactic acid-glycolic acid polymer is 5,000 to 50,000.
- 19. (Original) The method according to claim 15, wherein the weight average molecular weight of the lactic acid-glycolic acid polymer is 17,000 to 30,000.

- 20. (Original) The method according to claim 1, wherein the biodegradable polymer is a lactic acid polymer having a weight average molecular weight of 15,000 to 50,000 and the content of a polymer having a weight average molecular weight of 5,000 or less in said lactic acid polymer is 5% by weight or less.
- 21. (Original) The method according to claim 1, wherein the biodegradable polymer is a lactic acid-glycolic acid polymer having about 20 to about 1,000 µmol of terminal carboxyl per unit mass (gram) of the polymer.
- 22. (Original) The method according to claim 1, wherein the molar amount of the terminal carboxyl of the biodegradable polymer is about 0.1 to about 5 times that of the physiologically active substance.
- 23. (Original) The method according to any one of claims 1, 4 and 5, wherein the solution of a biodegradable polymer is prepared using a low water-soluble organic solvent.
- 24. (Original) The method according to claim 23, wherein the low water-soluble organic solvent is dichloromethane.
- 25. (Original) The method according to any one of claims 1, 4 and 5, wherein the mixture is a homogeneous mixture.
- 26. (Original) The method according to claim 25, wherein the homogenous mixture is an emulsion.
- 27. (Original) The method according to claim 26, wherein the emulsion is a W/O type emulsion.
- 28. (Original) The method according to claim 27, wherein the particle size of the W/O type emulsion.
- 29. (Original) The method according to claim 1, wherein the drying of the mixture is inwater drying.
- 30. (Original) The method according to claim 29, wherein an aqueous solution of an

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osmotic pressure regulating agent is used as an outer aqueous phase on the in-water drying.

- 31. (Original) The method according to claim 30, wherein the osmotic pressure regulating agent is mannitol.
- 32. (Original) The method according to claim 1, wherein the sustained-release composition is in the form of a microparticle.
- 33. (Original) The method according to claim 32, wherein the microparticle is a microsphere or a microcapsule.
- 34. (Original) A method for producing a sustained-release composition, which comprises mixing an aqueous solution containing 1) a physiologically active substance and 2) an acid or base in an amount of about 0.1 to about 20% by weight of said aqueous solution with a solution of a biodegradable polymer, and then drying the mixture.
- 35. (Original) The method according to claim 34, wherein the aqueous solution is obtained using a salt of the physiologically active substance with the acid or base.
- 36. (Original) A sustained-release composition produced by the method according to claim 1.
- 37. (Canceled)